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REISSUE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Reissue Application of:

U.S. Patent No.: 6,028,183

Issued: February 22, 2000

Serial No.: 08/966,392

Group Art Unit: 1623

Filing Date: November 7, 1997

Examiner: James O. Wilson

For: PYRIMIDINE DERIVATIVES AND OLIGONUCLEOTIDES CONTAINING
THE SAME

BOX REISSUE

Assistant Commissioner for Patents
Washington, D.C. 20231

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DATE OF MAILING: FEBRUARY 21, 2002

PRELIMINARY AMENDMENT IN APPLICATION FOR REISSUE

Applicants respectfully request that the above-identified reissue application be amended,
without prejudice, as follows.

In the Specification

Please amend the paragraph at column 12, lines 15-18, as follows:

Exemplary $-R^{2C}-R^{2D}$ and related structures are

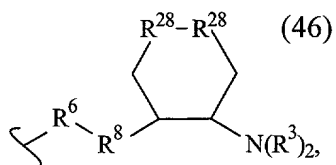
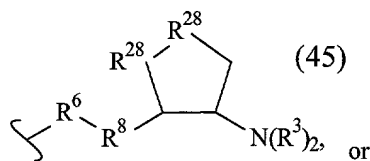
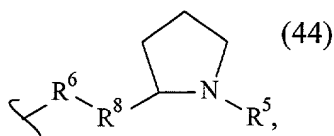
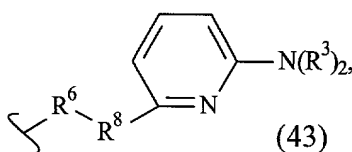
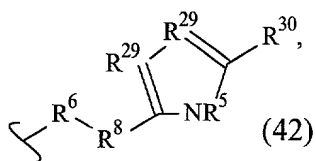
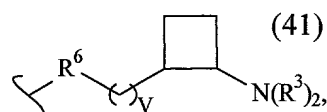
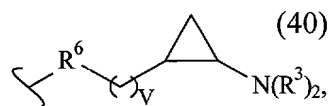
(a) $[-R^6-(CH_2)_t-NR^5C(NR^5)(NR^3)_2]$, including $-O-(CH_2)_t-NR^5C(NR^5)(NR^3)_2$, $-NH-(CH_2)_t-$
 $NR^5C(NR^5)(NR^3)_2$, and $-(CH_2)_{2-5}NR^5C(NR^5)(NR^3)_2$,]

$-\text{R}^6-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, including $-\text{O}-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, $-\text{NH}-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, and $-(\text{CH}_2)_{2-5}\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$

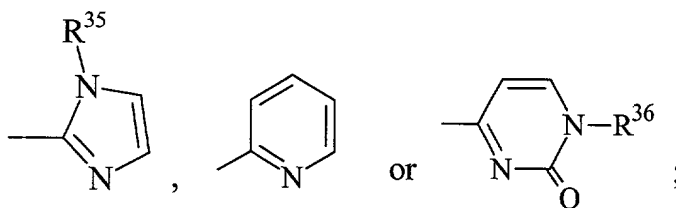
In the Claims:

Please amend claims 3, 4, 14, and 15 as follows:

3. (amended) The compound of claim 1, wherein R^2 is $[-\text{R}^6-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2]$
 $-\text{R}^6-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, $-\text{R}^6-\text{CH}_2-\text{CHR}^{31}-\text{N}(\text{R}^3)_2$, $-\text{R}^6-(\text{R}^7)_v-\text{N}(\text{R}^3)_2$, $-\text{R}^6-(\text{CH}_2)_t-\text{N}(\text{R}^3)_2$,
 $-(\text{CH}_2)_{1-2}-\text{O}-(\text{CH}_2)_t-\text{N}(\text{R}^3)_2$,



R^3 is independently -H, -CH₃, -CH₂CH₃, -(CH₂)_w-N(R³³)₂ or a protecting group, or both R^3 together are a protecting group, or when R^2 is -R⁶-(CH₂)_t-N(R³³)₂, one R^3 is -H, -CH₃, -CH₂CH₃, a protecting group or -(CH₂)_w-N(R³³)₂ and the other R^3 is -H, -CH₃, -CH₂CH₃, -(CH₂)_w-N(R³³)₂, -CH(N(R³³)₂)-N(R³³)₂,



R^5 is independently H or a protecting group;

R^6 is independently -S-, -NR⁵-, -O- or -CH₂-;

R^7 is independently linear alkyl having 1, 2, 3 or 4 carbon atoms optionally substituted with one -CH=CH-, -C=C- or -CH₂-O-CH₂- moiety, or R^7 is cyclic alkyl having 3, 4 or 5 carbon atoms, wherein one of the linear alkyl carbon atoms is optionally substituted with a single -CH₃, -CN, =O, -OH or protected hydroxyl, provided that the carbon atoms in any -CH=CH- or -CH₂-O-CH₂- moiety are not substituted with =O, -OH or protected hydroxyl;

R^8 is linear alkylene having 1 or 2 carbon atoms wherein one alkylene carbon atom is optionally substituted with a single -CH₃, -CN, =O, -OH or protected hydroxyl, or R^8 is absent;

R^{28} is independently -CH₂-, -CH(CH₃)-, -CH(OCH₃)-, -CH(OR⁵)- or -O-, but both are not -O-;

R^{29} is independently -N-, -N(CH₃)-, -CH-, -C(CH₃)-, but both are not -N(CH₃)-;

R^{30} is -H or $-N(R^3)_2$;

R^{31} is the side chain of an amino acid;

R^{33} is independently -H, $-CH_3$, $-CH_2CH_3$ or a protecting group;

R^{35} is H, C_1 - C_4 alkyl or a protecting group;

R^{36} is H, $-CH_3$, $-CH_2CH_3$, a protecting group or an optionally protected monosaccharide;

t is 1, 2, 3 or 4, but when R^6 is -O-, -S- or $-NR^5$ -, t is 2, 3 or 4;

v is independently 0, 1 or 2; and

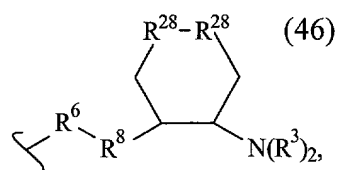
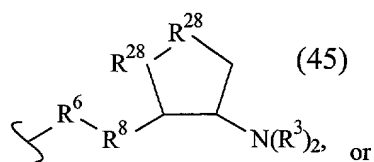
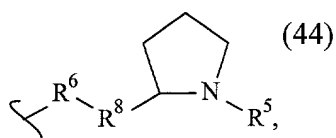
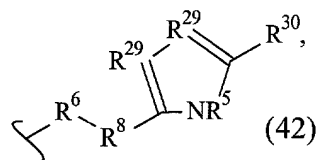
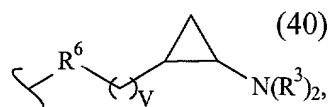
w is independently 1 or 2.

4. (amended) The compound of claim 3 wherein R^2 is $-CH_2-(CH_2)_tN(R^3)_2$,

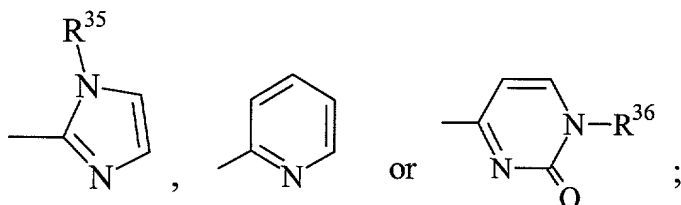
$-NR^5-(CH_2)_tN(R^3)_2$, $-S-(CH_2)_tN(R^3)_2$, $-O-(CH_2)_tN(R^3)_2$, $[-O-(CH_2)_tNR^5C(NR^5)(NR^3)_2]$, $-O-$
 $(CH_2)_tNR^5C(NR^5)N(R^3)_2$, $-(CH_2)_{1-2}-O-(CH_2)_tN(R^3)_2$, $-R^6-CH_2-CHR^{31}-N(R^3)_2$, $-R^6-(R^7)_v-N(R^3)_2$,
 $[-R^6-(CH_2)_t-NR^5C(NR^5)(NR^3)_2]$, $-R^6-(CH_2)_t-NR^5C(NR^5)N(R^3)_2$, or $[-CH_2-(CH_2)_tNR^5C(NR^5)(NR^3)_2]$,
 $-CH_2-(CH_2)_tNR^5C(NR^5)N(R^3)_2$.

14. (amended) The compound of claim 1, wherein R^2 is $[-R^6-(CH_2)_tNR^5C(NR^5)(NR^3)_2]$,

$-R^6-(CH_2)_tNR^5C(NR^5)N(R^3)_2$, $-R^6-CH_2-CHR^{31}-N(R^3)_2$, $-R^6-(R^7)_v-N(R^3)_2$, $-R^6-(CH_2)_t-N(R^3)_2$,
 $-(CH_2)_{1-2}-O-(CH_2)_tN(R^3)_2$,



R^3 is independently -H, -CH₃, -CH₂CH₃, -(CH₂)_w-N(R³³)₂ or a protecting group, or both R^3 together are a protecting group, or when R^2 is -R⁶-(CH₂)_t-N(R³³)₂, one R^3 is -H, -CH₃, -CH₂CH₃, a protecting group or -(CH₂)_w-N(R³³)₂ and the other R^3 is -H, -CH₃, -CH₂CH₃, -(CH₂)_w-N(R³³)₂, -CH(N(R³³)₂)-N(R³³)₂,



R^5 is independently H or a protecting group;

R^6 is independently -S-, -NR⁵-, -O- or -CH₂-;

R^7 is independently linear alkyl having 1, 2, 3 or 4 carbon atoms optionally substituted with one -CH=CH-, -C=C- or -CH₂-O-CH₂- moiety, or R^7 is cyclic alkyl having 3, 4 or 5 carbon atoms, wherein one of the linear alkyl carbon atoms is optionally substituted with a single -CH₃, -CN, =O, -OH or protected hydroxyl, provided that the carbon atoms in any -CH=CH- or -CH₂-O-CH₂- moiety are not substituted with =O, -OH or protected hydroxyl;

R^8 is linear alkylene having 1 or 2 carbon atoms wherein one alkylene carbon atom is optionally substituted with a single -CH₃, -CN, =O, -OH or protected hydroxyl, or R^8 is absent;

R^{28} is independently -CH₂-, -CH(CH₃)-, -CH(OCH₃)-, -CH(OR⁵)-, or -O-, but both are not -O-;

R^{29} is independently -N-, -N(CH₃)-, -CH-, -C(CH₃)-, but both are not -N(CH₃)-;

R^{30} is -H or -N(R³)₂;

R^{31} is the side chain of an amino acid;

R^{33} is independently -H, -CH₃, -CH₂CH₃ or a protecting group;

R^{35} is H, C₁-C₄ alkyl or a protecting group;

R^{36} is H, -CH₃, -CH₂CH₃, a protecting group or an optionally protected monosaccharide;

t is 1, 2, 3 or 4, but when R^6 is -O-, -S- or -NR⁵-, t is 2, 3 or 4;

v is independently 0, 1 or 2; and

w is independently 1 or 2.

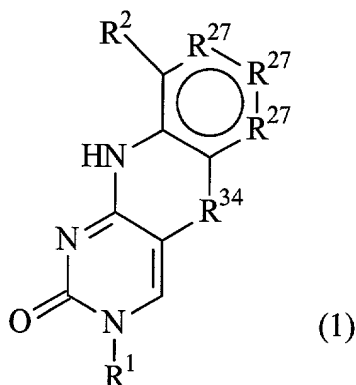
15. (amended) The compound of claim 14 wherein R^2 is $-\text{CH}_2-(\text{CH}_2)_t\text{N}(\text{R}^3)_2$, $-\text{NR}^5-(\text{CH}_2)_t\text{N}(\text{R}^3)_2$, $-\text{S}-(\text{CH}_2)_t\text{N}(\text{R}^3)_2$, $-\text{O}-(\text{CH}_2)_t\text{N}(\text{R}^3)_2$, $[-\text{O}-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2]$, $-\text{O}-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, $-(\text{CH}_2)_{1-2}-\text{O}-(\text{CH}_2)_t\text{N}(\text{R}^3)_2$, $-\text{R}^6-\text{CH}_2-\text{CHR}^{31}-\text{N}(\text{R}^3)_2$, $-\text{R}^6-(\text{R}^7)_v-\text{N}(\text{R}^3)_2$, $[-\text{R}^6-(\text{CH}_2)_t-\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2]$, $-\text{R}^6-(\text{CH}_2)_t-\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, or $[-\text{CH}_2-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2]$, $-\text{CH}_2-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$.

REMARKS

Claims 1-30 are pending in this reissue application. By way of this amendment, a portion of the specification and claims 3, 4, 14, and 15, have been amended. No claims have been added or canceled. U.S. Patent No. 6,028,183 (the 183 patent), which was filed on November 7, 1997 as U.S. application serial no. 08/966,392 (the 392 application), issued on February 22, 2000. This paper is being filed within two years of the issue date.

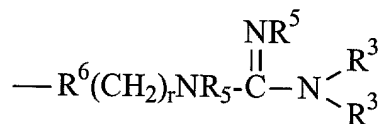
Applicants hereby seek reissue of the 183 patent because compound claims 3, 4, 14, and 15 erroneously contain substituent moieties that are technically incorrect. The amendments made herein are being made to correct this error.

In this regard, claim 3, which depends on claim 1, is directed to a compound of the formula:



wherein R^2 is defined as, among other things, the group $-R^6-(CH_2)_tNR^5C(NR^5)(NR^3)_2$ (*see*, the 183 patent at column 79, lines 1-2). The substituent group, as written, however, contains an insufficient number of chemical bonds to the nitrogen atoms due to the inadvertent misplacement of the parenthesis associated with the group $(NR^3)_2$. The recited structure is technically incorrect, as several of the nitrogen atoms are divalent.

Applicants have addressed this typographical error by amending claim 3 to recite the terminal portion of the R^2 substituent as $N(R^3)_2$. This amendment assures that the substituent contains the intended terminal guanidine functionality. The technically correct R^2 substituent may be represented structurally as:



Claims 4, 14, 15 also contain the inadvertent misplacement of the parenthesis associated with $\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$. For example, claim 4 recites, among other things, the groups $-\text{O}-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2$, $-\text{R}^6-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2$, and $-\text{CH}_2-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2$. Accordingly, Applicants have amended claim 4 to replace these structures with $-\text{O}-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, $-\text{R}^6-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, and $-\text{CH}_2-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, respectively. Claim 14 recites the group $-\text{R}^6-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2$. Applicants have amended claim 14 to replace this structure with $-\text{R}^6-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$. Claim 15 recites, among other things, the groups $-\text{O}-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2$, $-\text{R}^6-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2$, and $-\text{CH}_2-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2$. Applicants have amended claim 15 to replace these structures with $-\text{O}-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, $-\text{R}^6-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, and $-\text{CH}_2-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)\text{N}(\text{R}^3)_2$, respectively. The specification has also been amended, where appropriate, to correct the inadvertent placement of the parentheses in the guanidine functionality and to reflect the changes made to the foregoing claims.

Based on a straightforward chemical interpretation of $-\text{R}^6-(\text{CH}_2)_t\text{NR}^5\text{C}(\text{NR}^5)(\text{NR}^3)_2$, it is clear that the misplacement of the parenthesis is simply a typographical error. Thus, support for the requested amendments is implicit in the claims. Nevertheless, support for the amendments is also provided in the specification. For example, at column 45, lines 1-10, Applicants specifically describe guanidine functionalities as preferred R^2 groups. Accordingly, the requested changes do not introduce new matter and are fully supported by the application, as originally filed.

Claims 4, 5, 14, and 15, as amended herein, are fully commensurate with the disclosure of the 183 patent as well as the underlying 392 application. The error being corrected in this reissue application up to the time of filing of this declaration under 37 C.F.R. §1.175(a) arose without any deceptive intention on the part of the applicants and/or patentees.

In view of the foregoing, Applicants respectfully request approval of the changes to claim 3, 4, 14, and 15.

Respectfully submitted,



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